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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C12M 1/26, 1/12

A1

(11) International Publication Number: **WO 99/40175**

(43) International Publication Date: 12 August 1999 (12.08.99)

(21) International Application Number: PCT/CA99/00110

(22) International Filing Date: 9 February 1999 (09.02.99)

(30) Priority Data:
09/020,860 9 February 1998 (09.02.98) US

(71) Applicant *(for all designated States except US)*: ALBERTA RESEARCH COUNCIL [CA/CA]; 250 Karl Clark Road, Edmonton, Alberta T6N 6T4 (CA).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: WITTE, Lesley, D. [CA/CA]; 1407 Jefferys Cres, Edmonton, Alberta T6L 1Z4 (CA). YAU, Kelvin, Hing, Wah [CA/CA]; 10984–74 Avenue, Edmonton, Alberta T6G 0E6 (CA). GREY, Paul, Q. [CA/CA]; 1255–52 Street, Edmonton, Alberta T6L 1Z4 (CA).

(74) Agent: DEETH WILLIAMS WALL; National Bank Building, Suite 400, 150 York Street, Toronto, Ontario M5H 3S5 (CA).

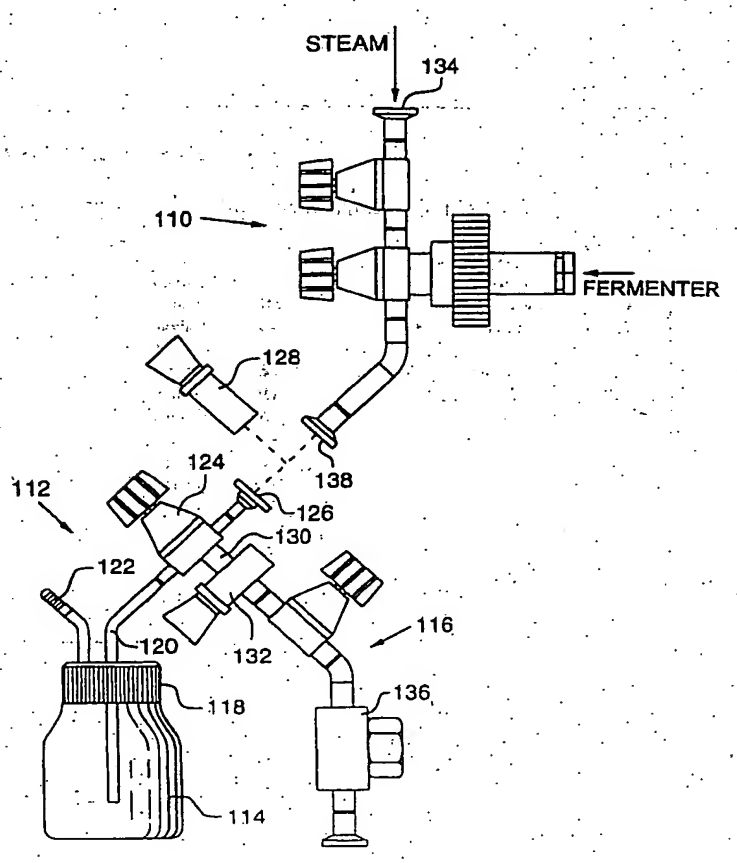
(81) Designated States: AU, CA, IN, JP, NZ, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: CONTAINED SAMPLING DEVICE

(57) Abstract

The contained sampling device of the present invention for taking sterile samples of a fluid such as biological samples from a fermenter or bio-reactor provides a simplified and completely contained system for collecting sterile samples. The contained sampling device includes a device body having a first fluid connection for connecting to a source of material to be sampled and a second fluid connection for connecting to a waste container. A bottle seat is provided on the device body for receiving a sampling bottle neck in fluid communication with the device body. First and second fluid paths extend through the device body for delivering fluid from the source of material to the sampling body or the waste container. Another embodiment of a sampling apparatus includes a sample collecting bottle holder in fluid communication with the fermenter or bio-reactor for removably connecting sample collecting containers. An adaptor is removably connected to the holder for steam sterilization of the holder between collection of successive samples. These systems for sterile sampling prevent contamination of the biological samples and also prevents exposure of workers to the sample media by allowing the purging of the sampling device after sample collection.



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CONTAINED SAMPLING DEVICE

BACKGROUND OF THE INVENTION

Field of the Invention:

The present invention relates to a contained sampling device for taking sterile samples and more particularly, to a sampling apparatus for removably attaching sample collecting containers to a fermenter or bio-reactor to withdraw uncontaminated samples from a sampling media.

Description of the Related Art:

Sterile sampling of fluids is performed periodically in many industries by removing a small fluid sample from a large batch or a continuous process into a sample collecting bottle for analysis. Such sterile sampling may include, for example, monitoring biological activity in fermenters or bio-reactors, testing liquid foods in the food processing industry, and monitoring water quality in water treatment plants.

Monitoring of biological activity in a fermenter is generally conducted by taking samples of the biological media within the fermenter at regular intervals over a period of time. For some processes it may be necessary to take such samples as often as about every fifteen minutes for proper monitoring of the process. Open sampling in which a liquid sample is drained into an uncovered sample bottle creates undesirable aerosols and the potential for contamination of the sample. Accordingly, enclosed sampling systems are generally preferred for collection of potentially hazardous materials.

An example of a known biological sampling apparatus for connection to a fermenter which reduces aerosol generation compared to open sample collection is illustrated in FIG. 1. According to the known assembly, an outlet pipe of the fermenter from which samples may be taken is connected to an outlet assembly 110 for connection of the sample taking apparatus. Connected to the outlet assembly 110 is a sampling assembly 112 including a sample collecting bottle 114. The sampling assembly 112 is also removably connected to a steam trap assembly 116.

The known sampling assembly 112 includes the bottle 114 having a cap 118, an inlet tube 120, and a vent 122 extending through the cap 118 with a filter provided in the vent. Connected to the inlet tube 120 is a three way valve 124 for directing fluid to the bottle 114 and steam to the steam trap 136. The sampling assembly 112 has a first connection end 126 for connection by a tri-clamp 128 to an end 138 of the outlet assembly 110 and a second connection end 130 shown connected by a second tri-clamp 132 to the steam trap assembly 116.

In order to take a sample with the known sample taking apparatus of FIG. 1, the entire sampling assembly 112 including the bottle 114, the valve 124, and the two connection ends 126, 130 is autoclaved prior to use. This sampling assembly 112 is then connected to the outlet assembly 110 of the fermenter and to the steam trap assembly 116 by the tri-clamps 128, 132. Once the sampling assembly 112 has been attached by the tri-clamps 128, 132, steam is passed from a steam inlet 134 to the sampling assembly 112 and through a portion of the sampling assembly into the steam trap 136. This steam sterilization process is conducted for about fifteen to twenty minutes to sterilize the inlet pipe and valve 124 of the sampling assembly 112. After this steam sterilization step, a biological sample is withdrawn from the fermenter through the outlet assembly 110 and sampling assembly 112 into the bottle 114. During sample collection, air escapes from the bottle 114 through the bottle vent 122 which has a filter attached. The sampling assembly 112, including the bottle 114, cap 118, and valve 124 are then disconnected by the tri-clamps 128, 132 from the fermenter and the steam trap 136 and a new sampling assembly 112 may be attached for withdrawal of a subsequent sample.

One of the drawbacks of this known sample taking system is the complicated and cumbersome system of valves and tubes required. Further, this system does not provide for cooling of the sampling assembly after the heating caused by the steam sterilization step.

It would be desirable to provide a compact contained sampling device which is easily attached and detached from a fermenter or other sample source and allows cooling of the sampling assembly.

SUMMARY OF THE INVENTION

The present invention relates to a completely contained and simplified sampling device for taking biological samples from a fermenter, bio-reactor, or other sample source which can be used to take samples without exposing workers to the sample media.

In accordance with one aspect of the present invention, a contained sampling device for collecting samples includes a device body having a first fluid connection adapted to be connected to a source of material to be sampled and a second fluid connection adapted to be connected to a waste container or kill tank. A bottle seat is provided on one surface of the device body for receiving a bottle in fluid communication with the device body. A first fluid path extends through the device body from the first fluid connection to the second fluid connection. A second fluid path extends through the device body from the first fluid connection to the bottle seat. A first valve is provided in the first fluid path and a second valve is provided in the second fluid path.

In accordance with another aspect of the present invention, a method for collecting biological samples with a contained sampling device includes steps of installing a bottle in a bottle seat of the contained sampling device, autoclaving the contained sampling device and bottle, connecting an inlet of the contained sampling device to a source of biological samples, and connecting an outlet of the contained sampling device to a waste container. A first valve in the contained sampling device is opened to steam an interior of the sampling device. A second valve in the contained sampling device is opened to collect a biological sample in the bottle. The first valve in the contained sampling device is reopened to purge the sampling device with steam. The contained sampling device is disconnected from the biological sample source and the waste container or kill tank. The bottle is then removed from the contained sampling device in a biosafety hood.

In accordance with a further aspect of the present invention, a method for collecting samples with a contained sampling device includes installing a bottle in a bottle seat of the contained sampling device, connecting an inlet of the contained sampling device to a source of sample material and connecting a waste outlet of the

contained sampling device to a waste container or kill tank, opening a first valve in the contained sampling device to steam an interior of the sampling device, cooling the sampling device by allowing the sample material to pass through the sampling device from the inlet to the waste outlet, and collecting a sample by opening a second valve to allow the sample material to flow from the inlet into the bottle from the sampling device.

According to another aspect of the present invention, a sampling apparatus for collecting sterile samples includes a holder in fluid communication with a source of material to be sampled. The holder has a substantially cylindrical interior surface and a substantially cylindrical exterior surface. An attachment mechanism is provided on the substantially cylindrical exterior surface. An adaptor for connecting the holder to a steam trap is attachable in a fluid tight manner to the attachment mechanism on the exterior surface of the holder to allow steam sterilization of the holder. A sterilized sample collecting container is received in a container receiving seat formed on the substantially cylindrical interior surface of the holder.

According to an additional aspect of the present invention, a holder system for sample collecting containers includes a cup shaped holder body having an interior surface, an exterior surface, and an inlet. A container receiving seat is formed by the interior surface of the holder body for removably receiving sample collecting containers in a fluid tight manner. An attachment mechanism is formed on the exterior surface of the holder body for receiving an adapter for connecting the holder body to a steam trap for sterilization of the container receiving seat.

According to another aspect of the present invention, a method for collecting biological samples from a biological media includes steps of connecting a steam sterilization adapter to an exterior surface of a sample container holder, steam sterilizing an interior surface of the sample container holder by passing steam through the sample container holder and the adapter, removing the steam sterilization adapter from the sample container holder, connecting a sterilized sample collecting container to the sample container holder, and withdrawing a biological sample from the biological media into the sample collecting container.

BRIEF DESCRIPTION OF THE DRAWING FIGURES

The invention will be described in greater detail with reference to the accompanying drawings in which like elements bear like reference numerals, and wherein:

FIG. 1 is a side view of a known biological sample collecting apparatus;

FIG. 2 is an exploded front view of the contained sampling device according to the present invention;

FIG. 3 is a left side view of the contained sampling device of FIG. 2;

FIG. 4 is a right side view of the contained sampling device of FIG. 2;

FIG. 5 is an exploded top view of the contained sampling device of FIG. 2;

FIG. 6 is a side view partly in cross section of an alternative embodiment of a sampling apparatus according to the present invention with an adapter connected to a sample holder;

FIG. 7 is a side view partly in cross section of the sampling apparatus of FIG. 6 with a sample collecting container attached to the adapter;

FIG. 8 is a side cross sectional view of an alternative embodiment of the sample container holder and adapter of FIG. 6; and

FIG. 9 is a side cross sectional view of the sample container holder of FIG. 8 with a sample bottle for connection to the holder.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention provides a simplified, compact, and fully contained system for collecting biological samples from a fermenter or bio-reactor which prevents contamination of the biological samples. The fully contained system also prevents exposure of workers to the sample media before, during, or after sample collection. Although the present invention will be described in detail as it is used with a fermenter or bio-reactor, the invention may also be used in other industries where periodic sampling of a processed liquid is desired, such as, in the liquid food processing industry, water treatment industry, and the like.

FIG. 2 illustrates an exploded front view of a contained sampling device 10 according to the present invention. The sampling device 10 includes a device body 12 and first and second valve bonnets 14, 16 secured to the body on opposite sides. The device body 12 includes a cylindrical bottle seat 20 formed in a lower portion of the body and having internal threads 22 for receiving the threaded neck of a sampling bottle. The device body 12 includes internal fluid paths for use in both purging the device body and filling the sampling bottle connected to the bottle seat 20. As illustrated in the top view of FIG. 5, the device body 12 is substantially rectangular in shape and is connected to a substantially cylindrical bottle seat 20.

Although the arrangement of the fluid paths and the valves in the contained sampling device 10 according to the present invention have been illustrated and described to be arranged in a particular exemplary configuration, it should be understood that the fluid paths and valves may take on other arrangements without departing from the present invention. For example, the valve bonnets 14, 16 are illustrated to be on opposite sides of the body 12 but may both be positioned on the same side of the device body.

The device body 12 includes a biological sample inlet 24 having a flange 26 for connection by a tri-clamp to an outlet pipe of a fermenter or bioreactor in which the biological media is contained. The device body 12 also includes a waste outlet 28 having a flange 30 for connection by a tri-clamp to a waste container or steam trap. Although the sample inlet 24 and the waste outlet 28 have been illustrated as including annular flanges for connection by tri-clamps to adjoining pipes, it should be understood that other types of removable pipe connections or fittings may also be used including quick connect couplings, threaded joints, or the like.

A first fluid path 32 extends through the device body 12 of the sampling device from the sample inlet 24 to the waste outlet 28. Flow through the first fluid path 32 is controlled by the rotating a knob 42 of the first valve bonnet 14. A second fluid path 34 extends through the device body 12 from the sample inlet 24 to the bottle seat 20. Flow through the second fluid path 34 is controlled by rotating a knob 44 of the second valve bonnet 16. Although the valves have been illustrated as manual valves, pneumatically

operated valves, electrically operated valves, or other known automatic or manual valves may be used.

The flange 26 of the sample inlet 24 is adapted to be connected by a tri-clamp to an outlet pipe of a fermenter or bio-reactor for collection of biological samples. The outlet of the fermenter or bio-reactor also includes a steam supply and associated valve for delivery of steam to the contained sampling device 10. The fermenter steam supply allows steam to pass into the sample inlet 24 of the device body 12 for the purpose of steam sterilization and purging of the device body. One example of a fermenter outlet assembly 110 with a steam supply is illustrated in the prior art embodiment of FIG. 1.

The first and second fluid paths 32, 34 each include a concave valve seat 36, 38, respectively, which form a part of the first and second fluid paths. The valve bonnets 14, 16 are secured to the device body 12 over the concave valve seats 36, 38 by threaded fasteners inserted in bores 40 in the valve bonnets. The valve bonnets 14, 16 each include a diaphragm (not shown) and a rotatable valve knob 42, 44. Rotation of the valve knobs 42, 44 move the diaphragms between a closed position and an open position. In the closed position, the diaphragms of the valve bonnets 14, 16 seat in a fluid tight manner in the concave valve seats 36, 38 of the device body 12 to block the associated fluid path 32, 34. In the open position, the fluid passes between the concave valve seats 36, 38 and the diaphragms.

The diaphragm valves used in the present invention are a type of sanitary valve. Sanitary valves are those providing no areas which allow contamination to become trapped within the valve. An example of a non-sanitary valve would be a ball valve which allows particles to become trapped in the closed valve and releases the particles upon opening the valve. The diaphragm valves illustrated in the figures can be replaced by other types of valves. However, the valves for use in the present invention are preferably sanitary type valves. One example of a valve bonnet is the manually actuated diaphragm valve available from Bioengineering AG of Switzerland.

The bottle seat 20 having the internal threads 22 is preferably provided with an internal groove 47 having at least one O-ring 48 to provide a fluid tight seal between the

neck of the sampling bottle and the bottle seat. The O-ring 48 may be formed of any known autoclavable seal material. The size of the bottle seat 20 and configuration of the internal threads 22 may vary depending on the size and type of bottle to be used. However, preferably, the bottle seat 20 is configured to receive standard sampling bottle sizes such as the Pyrex Brand reusable bottles, or Kimble borosilicate glass bottles having 33 mm threaded necks.

The bottle seat 20 also includes a vent 50 extending through the device body 12 from an interior of the bottle seat to an exterior of the device body. The vent 50 allows gas to exit the sampling bottle while the sample is being collected. A filter is preferably secured into a threaded portion 52 of the vent. The filter is preferably a 1 μm or smaller, and more preferably a 0.2 μm or smaller reusable, autoclavable filter. Examples of filters which may be used include the Acro 50 vent devices available from Gelman Sciences of Ann Arbor, Michigan, U.S.A. These disk shape filters are designed with different types of connections such as a hose barb inlet end which can be inserted within a flexible hose or other orifice. Preferably, the filter is provided with a threaded connection which is threaded into the appropriately sized threaded portion 52 of the vent hole 50 such that the gas exiting the sampling bottle through the vent hole passes through the filter to remove contaminants prior to exiting into the environment.

One example of a sequence for operating the contained sampling device to collect samples according to the present invention is described below. This operating procedure allows for the collection of sterile samples in sample collection bottles and prevents environmental contamination when the bottle containing the sample is removed from the sampling device. Initially, both valve knobs 42, 44 are rotated to a closed position and a filter is installed in the vent 50 of the device body 12 with a direction of flow away from the device body. The O-ring 48 is checked to ensure that it is in place in the groove 47 at the base of the bottle seat 20. A precleaned autoclavable sampling bottle is installed in the bottle seat 20. The contained sampling device 10 and connected bottle are placed in an autoclave and sterilized. The autoclaving step may vary depending on the system. One example of an autoclaving process provides sufficient sterilization for most

procedures by sterilization at approximately 120° C, preferably about 121° C for a minimum of thirty minutes. Alternatively, other sterilization techniques, temperature, and times may be used in accordance with normal procedures for the particular facility involved.

After the contained sampling device 10 with connected sampling bottle has been autoclaved the sampling device is attached to a vessel sample port of a fermenter, bio-reactor, or other source with the sample inlet 24 connected to the sample port of the fermenter. The waste outlet 28 of the sampling device 10 is connected to a vented waste container or kill tank that is capable of receiving live steam. The waste container or kill tank should be equipped with a suitable filter, such as a 0.2 μm absolute rated vent filter, to protect the environment. The waste container or kill tank may also be equipped with a shutoff valve adjacent to the connection 30 to the device body 12 for isolation purposes.

Once the sampling device 10 has been properly connected to the fermenter and the waste container, the steam supply from the fermenter is turned on. The first valve knob 42 is then partially opened and adjusted to allow a steady wisp of steam to flow through the first fluid path 32 through the device body 12 and into the waste container. The steam flow is maintained for about 30 minutes or more. Alternatively, the steam sterilization may be performed according to the normal procedures for the facility. The steam supply is then turned off and the first valve knob 42 is turned to the completely open position. The fermenter sample valve is then opened to allow a sufficient quantity of sample media to flow through the device body 12 into the waste container or kill tank to cool the sample valve assembly. This cooling step is needed only when temperature sensitive samples are to be collected. For non-temperature sensitive samples, the cooling step may be omitted.

Once the device body 12 has been cooled the first valve knob 42 is turned to an off position and the second valve knob 44 is opened to allow flow of the biological sample media through the second fluid path 34 from the fermenter into the sampling bottle. Once the sample has been collected in the bottle the second valve knob 44 is turned off and the fermenter sample valve is also turned off.

Steam is then supplied to the device body 12 to purge the device body by turning on the steam supply of the fermenter and partially opening the first valve knob 42 to allow a steady wisp of steam and condensate to pass through the device body through the first fluid path 32 to the waste container. The steam flow is maintained again for about 30 minutes or more, or according to normal procedures for the facility.

Once the steam purging operation is completed the fermenter system steam supply, the first valve knob 42, and the waste container valve are closed and the device body 12 is disconnected from the waste container or kill tank line at the waste outlet 28. The device body 12 is also disconnected from the fermenter or bio-reactor at the sample inlet 24. The disconnected contained sampling device 10 with the filled sampling bottle connected thereto, once disconnected from the fermenter and the waste container or kill tank does not present a contamination risk to workers because the exposed portions of the device body have been purged by steaming. The sampling device 10 and connected filled sampling bottle are removed together to a biosafety hood in which the sampling bottle is removed from the device body 12 and a presterilized cap is placed on the sampling bottle.

The foregoing procedure provides a sampling method in which the sample sterility is ensured and the sample media is never allowed to contaminate the environment or create hazardous aerosols for workers. However, the contained sampling device 10 according to the present invention may also be used for non-hazardous substances in which case the contained sampling device is not removed to a biosafety hood to remove and cap the sample bottle. With these non-hazardous materials, the sample bottle may be unthreaded from the device body 12 with the valves 42, 44 closed and the device body still connected to the fermenter and the waste container.

According to an alternative embodiment of the invention, a method for using the contained sampling device 10 with less hazardous substances may use an adapter for steam sterilization of the contained sampling device in a manner which is described below with respect to FIGS. 6-9. The adaptor is connected over the bottle seat 20 and allows steam to pass through the device body 12 and bottle seat 20 and into a steam trap

connected to the adaptor to steam sterilize the contained sampling device 10 prior to connection of a sampling bottle.

FIG. 6 illustrates an alternative embodiment of a sampling apparatus according to the present invention including a biological sample inlet 52 having a flange 54 for connection by a tri-clamp to an outlet pipe of a fermenter or bio-reactor, in which a biological media is contained. The sample inlet 52 is connected by a pipe 48 to a three-way valve 56. The three-way valve 56 is connected by a pipe 58 to a sample container holder 60 and is also connected to a waste discharge pipe 62.

The sample container holder 60 includes an external substantially cylindrical threaded surface for connection to an adapter 70. The sample container holder 60 also includes a substantially cylindrical threaded interior surface 66 for fluid tight connection to a sample collecting container.

The adapter 70 is a funnel shaped device which is connected to the exterior of the sample container holder 60 for steam sterilization of the sample container holder. The adapter 70 includes an internal threaded surface 72 for engagement with a threaded exterior surface 64 of the sample container holder 60. The adapter 70 also includes a conical portion 74 and a bottom flange 76 for connection of the adapter to a steam trap by a tri-clamp. A sealing member in the form of an annular gasket 80 is preferably provided between a lower surface of the sample container holder 60 and the adapter 70 to provide a fluid tight seal between the adapter and the container holder.

FIG. 7 illustrates the sampling apparatus with the adapter 70 removed and a sample collecting container 90 attached to the sample container holder 60 for withdrawal of a biological sample. Although the present invention has been illustrated with a sample collecting container 90 in the form of a bottle, it should be understood that the invention may be used with a sampling container of any shape, such as a tube, a vial, a bottle, or the like. The internal threads 66 of the sample container holder 60 may be modified to fit containers of these different configurations. As shown in FIG. 7, the sample collecting container 90 according to one variation of the present invention has an externally

threaded neck 92 which forms a fluid tight seal with the threaded interior surface 66 of the sample container holder 60.

In operation, the sample collection system according to FIGS. 6 - 9 is used as follows. Initially, the interior surfaces of the sample container holder 60, the valve 56, and pipes 48, 58 are steam sterilized. Sterilization is performed by connection of the adapter 70 to the sample container holder 60 and passing steam from the sample inlet 52 through the three-way valve 56, the sample container holder 60, and the adapter 70 to a steam trap connected to the bottom flange 76 of the adapter. This steam sterilization is preferably performed for about fifteen to twenty minutes to ensure that substantially all contamination is eliminated. The connection of the adapter 70 to an exterior of the sample container holder 60 ensures that the interior walls of the holder including the threads 66 are adequately sterilized.

After the steam sterilization step, the steam to the assembly is turned off so that steam no longer enters through the sample inlet 52. The three-way valve is then turned to divert flow from the fermenter through pipe 48 to the waste discharge through the waste discharge pipe 62. The sample valve on the fermenter or bio-reactor is opened allowing the sample broth to be diverted to a waste container to cool the sample assembly. Once the sample assembly is cool the three-way valve 56 is turned to the closed position. The adapter 70 is removed from the sample holder 60 and a sterile sample collecting container 90 is attached to the sample container holder as shown in FIG. 7. The biological sample is withdrawn into the sample container 90 by opening the three-way valve 56 to divert flow to the sample container 60.

After the sample has been collected the three-way valve 56 is turned to the closed position and the sample valve on the fermenter or bio-reactor is also closed. The sample container 90 is removed from the holder 60 and immediately covered with a sterilized cap to minimize aerosol generation. The three-way valve 56 is then diverted to the waste container through the waste pipe 62 and the steam is turned on from the fermenter or bio-reactor to steam out fluid remaining in the inlet pipe 48 and the valve 56 of the sampling assembly. The adapter 70 is then reconnected to the sample container holder

60. A steam trap is connected at 76 to the adapter 70 and the three-way valve 56 is turned to divert steam through the sample inlet 52, the three-way valve 56, the sample container holder 60, and the adapter 70 to a steam trap connected to the adapter 76 to steam out the holder 60.

The adaptor 70 is shaped as a funnel because the funnel shape is self-draining and will not allow fluid to accumulate within the adaptor causing possible contamination. Other adaptor shapes which are self-draining may also be used without departing from the present invention. According to one preferred embodiment, the adaptor 70 tapers from a first diameter at its upper end to a second diameter which is approximately one-quarter of the first diameter. For example, the adaptor 70 may have an upper diameter of about 2 inches and a lower diameter of about ½ inch.

The present invention has been illustrated without a vent structure in the sample container holder 60 or the container 90. Although no vent is needed for relatively slow or moderate rates of flow into the container 90, for higher flow rates a vent may be added which allows air to escape as the container 90 is filled. The vent would preferably include a filter to prevent aerosol generation.

FIGS. 8 and 9 illustrate an alternative embodiment of the present invention in which alternative embodiments of the attachment mechanisms for attachment of the adaptor and the container to the holder are employed. In particular, the sample container holder 60a of FIG. 8 includes an external flange 96 for connection of the adapter 70a by a clamping device (not shown) such as a tri-clamp. As shown in FIG. 8, the adapter 70a has a annular flange 100 which corresponds to the external flange 96 of the sample container holder 60a for connection by the clamping device.

The sample container holder 60a of FIGS. 8 and 9 also includes an internal rib 98 with a hemispherical cross section which provides a snap fit with the sample collecting container 90a. As shown in FIG. 9, the sample collecting container or bottle 90a has an external groove 102 in the neck. The external groove 102 has a hemispherical concave cross section which corresponds with that of the rib 98. According to the embodiment of FIGS. 8 and 9, preferably, the sample container holder 60a and/or the neck of the sample

collecting container 90a are resilient to allow the sample collecting container to be snapped into the sample container holder in a fluid tight manner.

The present invention has been described as employing threaded, snap fitting, or clamped connections between the sample container holder 60, 60a, the sample collecting container 90, 90a, and the adapter 70, 70a. However, it should be understood that other attachment mechanisms may also be used without departing from the scope of the present invention.

The sample container holder 60 and the adaptor 70 according to the present invention are preferably formed of stainless steel which can be autocalved periodically. The invention may also employ other materials such as the resilient materials used in the snap fit embodiment.

While the invention has been described in detail with reference to the preferred embodiments thereof, it will be apparent to one skilled in the art that various changes and modifications can be made, and equivalents employed, without departing from the spirit and scope of the invention.

What is claimed is:

1. A contained sampling device for collecting sterile samples comprising:

a device body having a first fluid connection adapted to be connected to a source of material to be sampled and a second fluid connection adapted to be connected to a waste container or kill tank;

a bottle seat provided on one surface of the device body for receiving a bottle in fluid communication with the device body;

a first fluid path extending through the device body from the first fluid connection to the second fluid connection;

a second fluid path extending through the device body from the first fluid connection to the bottle seat;

a first valve provided in the first fluid path; and

a second valve provided in the second fluid path.

2. The contained sampling device of Claim 1, further comprising a vent extending through the device body from an interior of the bottle seat to an exterior of the device body and a filter connected to the vent.

3. The contained sampling device of Claim 2, wherein the filter is an autoclavable 1 μm or smaller filter.

4. The contained sampling device of Claim 1, wherein the bottle seat includes internal threads and an O-ring for providing a seal between the device body and a bottle neck of a sample collecting bottle which is received in the bottle seat for collection of sterile samples.

5. The contained sampling device of Claim 1, wherein the first and second valves are sanitary valves which do not allow particulates to become caught in the valve mechanism.

6. The contained sampling device of Claim 1, wherein the first and second valves are diaphragm valves.

7. The contained sampling device of Claim 6, wherein the first and second fluid paths each include a concave surface which receives a diaphragm of one of the first or second diaphragm valves to close the fluid paths.

8. The contained sampling device of Claim 1, wherein the first and second fluid paths and the bottle seat are formed by bores cut into the device body, and wherein the device body is a single unitary member.

9. The contained sampling device of Claim 1, wherein the first and second valves each include a concave valve seat cut into the device body, and a valve bonnet having a diaphragm and a rotatable valve knob, and wherein the valve bonnet is fixed to the device body at a location of the valve seat.

10. A method for collecting biological samples with a contained sampling device comprising:

installing a bottle in a bottle seat of the contained sampling device;

autoclaving the contained sampling device and bottle;

connecting an inlet of the contained sampling device to a source of biological samples and connecting an outlet of the contained sampling device to a waste container or kill tank;

opening a first valve in the contained sampling device to steam an interior of the sampling device;

closing the first valve;

opening a second valve in the contained sampling device to collect a biological sample in the bottle;

closing the second valve;

opening the first valve in the contained sampling device to purge the sampling device with steam;

disconnecting the contained sampling device from the biological sample source and the waste container; and

removing the bottle from the contained sampling device in a biosafety hood.

11. The method for collecting biological samples of Claim 10, wherein the step of autoclaving includes sterilizing at approximately 121°C for at least thirty minutes.

12. The method for collecting biological samples of Claim 10, wherein the step of steaming the contained sampling device includes delivering steam for at least about thirty minutes.

13. The method for collecting biological samples of Claim 10, wherein prior to collecting the biological sample, the contained sampling device is cooled by opening the first valve and allowing a biological sample material to pass through the contained sampling device to the waste container or kill tank.

14. The method for collecting biological samples of Claim 10, wherein the step of purging the contained sampling device involves delivering steam for at least about thirty minutes.

15. A method for collecting samples with a contained sampling device comprising:

installing a bottle in a bottle seat of the contained sampling device;

connecting an inlet of the contained sampling device to a source of sample material and connecting a waste outlet of the contained sampling device to a waste container or kill tank;

opening a first valve in the contained sampling device to steam an interior of the sampling device;

cooling the sampling device by allowing the sample material to pass through the sampling device from the inlet to the waste outlet;

collecting a sample by opening a second valve to allow the sample material to flow from the inlet into the bottle from the sampling device.

16. A sampling apparatus for collecting sterile samples comprising:

a holder in fluid communication with a source of material to be sampled, the holder having an interior surface and an exterior surface;

an attachment mechanism on the exterior surface;

an adaptor for connecting the holder to a steam trap, the adaptor attachable in a fluid tight manner to the attachment mechanism on the exterior surface of the holder to allow steam sterilization of the holder;

a sterilized sample collecting container having a container neck; and

a container receiving seat formed on the interior surface of the holder for removably receiving the sample collecting container in a fluid tight manner.

17. The sampling apparatus according to Claim 16, wherein the attachment mechanism includes external threads on the exterior surface of the holder.

18. The sampling apparatus according to Claim 17, wherein the container receiving seat includes internal threads for threadably receiving the sample collecting container.

19. The sampling apparatus according to Claim 16, wherein the exterior surface is concentric with and surrounds the interior surface of the holder.

20. The sampling apparatus according to Claim 16, wherein the adaptor has a tapered shape which is self-draining.

21. The sampling apparatus according to Claim 16, wherein the holder body is removably attached to a fermenter to withdraw the sterile samples.

22. A holder system for sample collecting containers comprising:

a cup shaped holder body having an interior surface, an exterior surface, and an inlet;

a container receiving seat formed by the interior surface of the holder body for removably receiving sample collecting containers in a fluid tight manner; and

an attachment mechanism formed on the exterior surface of the holder body for receiving an adaptor for connecting the holder body to a steam trap in a fluid tight configuration for sterilization of the sample collecting container receiving seat.

23. The holder system according to Claim 22, wherein the container receiving seat is threaded to receive a threaded sample collecting container neck.

24. The holder system according to Claim 22, wherein the container receiving seat includes a snap fit connection for receiving a sample collecting container neck.

25. The holder system according to Claim 22, wherein the attachment mechanism formed on the substantially cylindrical exterior surface of the holder body includes external threads which cooperate with internal threads on the adaptor.

26. The holder system according to Claim 22, wherein the attachment mechanism formed on the substantially cylindrical exterior surface of the holder body includes a flange for connections by a clamping mechanism.

27. The holder system according to Claim 22, further comprising a resilient sealing member for sealing between the holder body and the adapter during steam sterilization of the holder body.

28. A method for collecting biological samples from a biological media comprising:

connecting a steam sterilization adaptor to an exterior surface of a sample container holder of a sampling apparatus;

steam sterilizing an interior surface of the sample container holder by passing steam through the sample container holder and the adaptor;

removing the steam sterilization adaptor from the sample container holder;

connecting a sterilized sample collection container to the interior surface of the sample container holder; and

withdrawing a biological sample form the biological media into the sample collecting container.

29. The method for collecting biological samples according to Claim 28, wherein the steam sterilization step includes passing the steam through the sample container holder and the adapter into a steam trap connected by the adaptor to the holder.

30. The method for collecting biological samples according to Claim 28, wherein the sample collecting container is connected to the sample container holder by threading a neck of the container into the holder.

31. The method for collecting biological samples according to Claim 28, wherein the steam sterilization adaptor is connected to the sample container holder by threading a mouth of the adaptor onto the holder.

32. The method for collecting biological samples according to Claim 28, wherein the samples are withdrawn from a fermenter.

33. The method for collecting biological samples according to Claim 28, wherein after the steam sterilization step cooling is performed by allowing the biological media to flow through the sample apparatus.

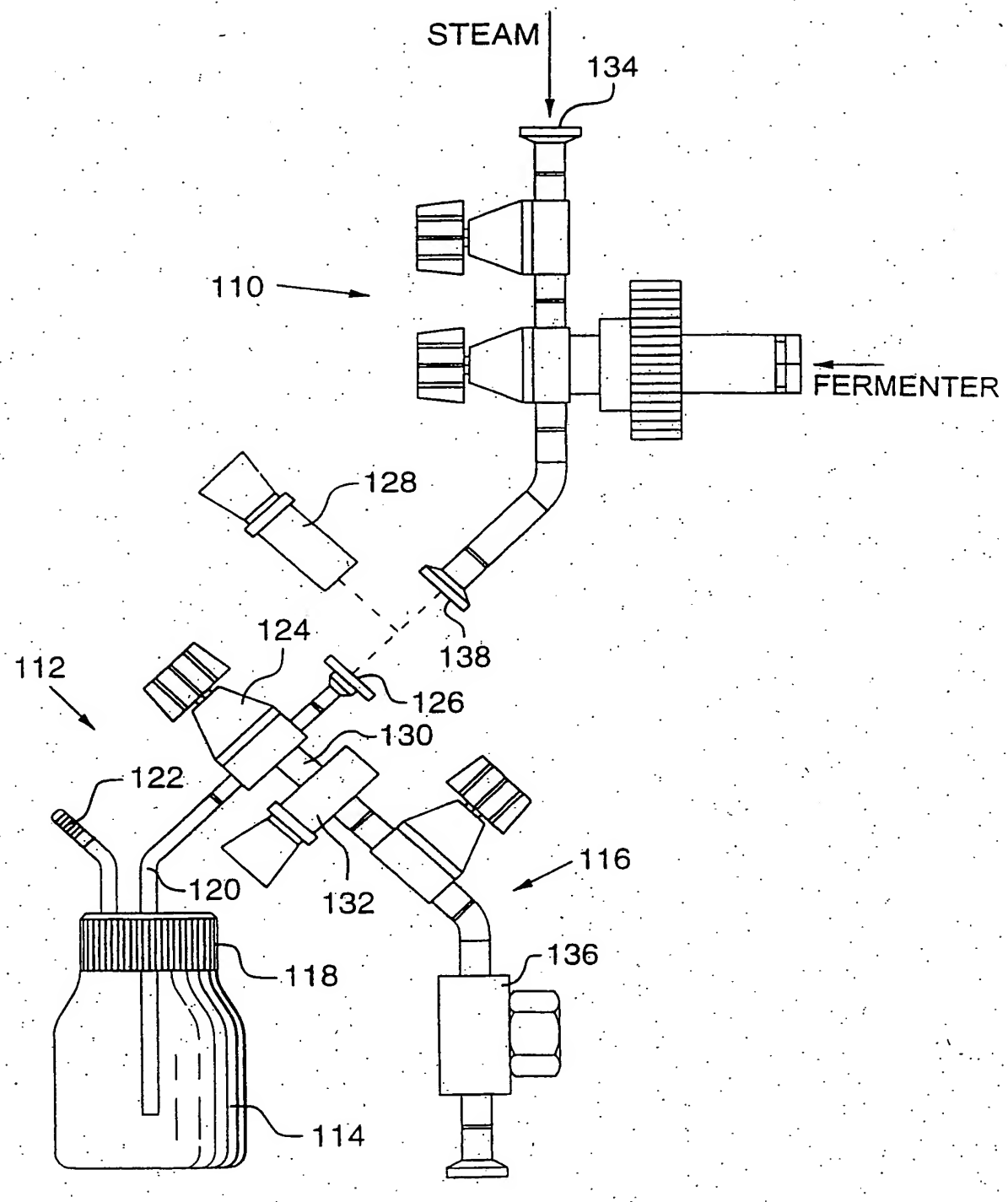

FIG.1
PRIOR ART

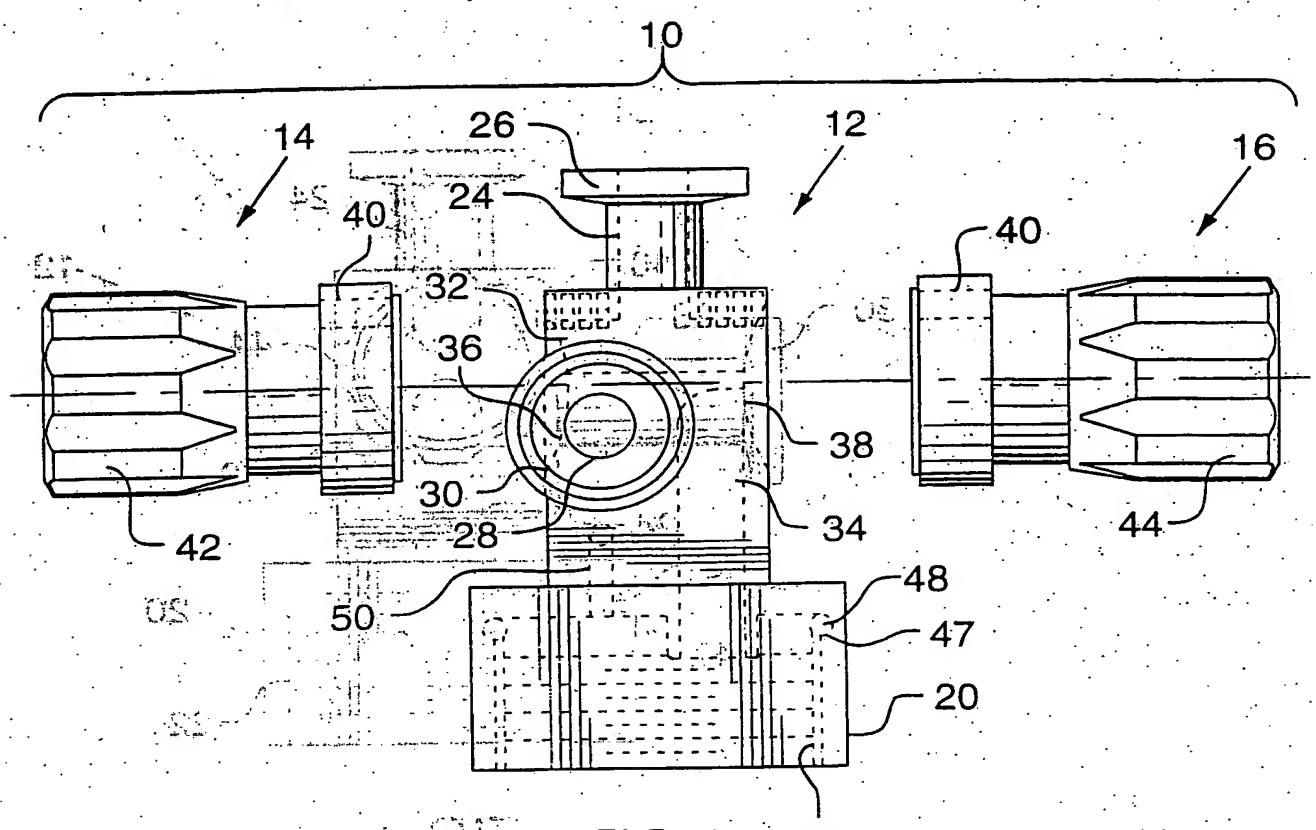
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FIG.2

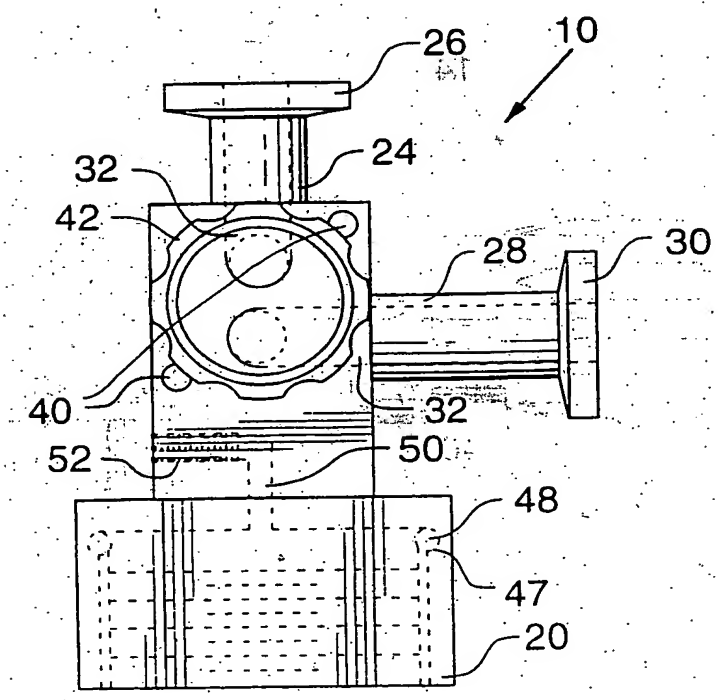
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FIG.3

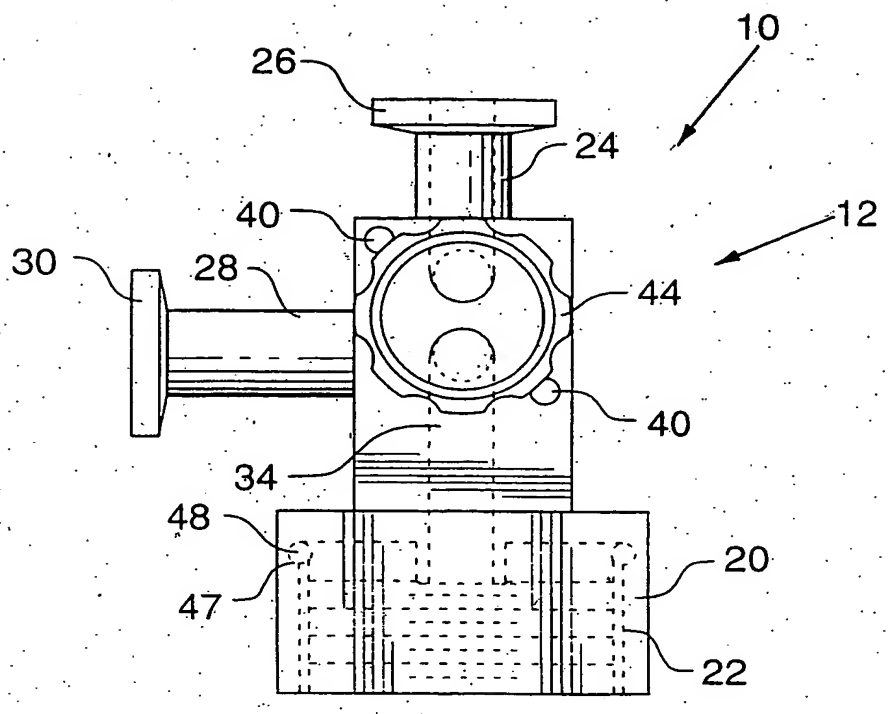
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FIG.4

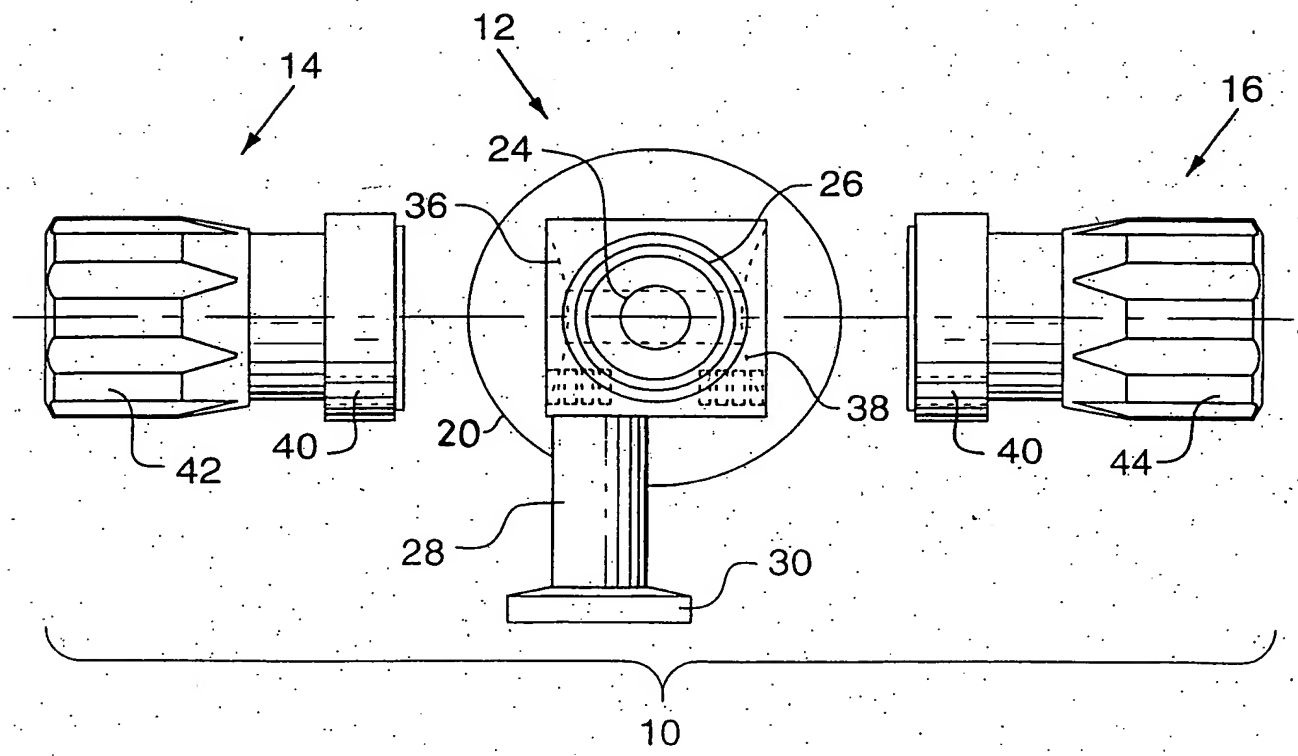
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FIG.5

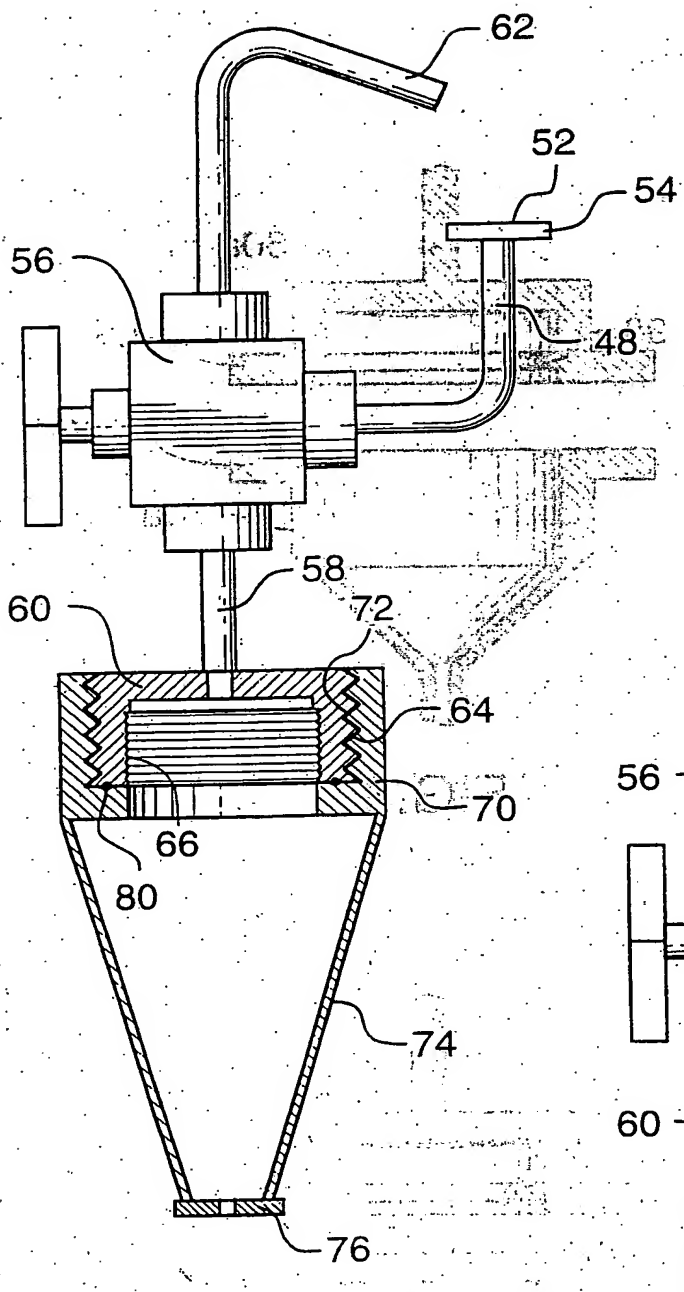
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FIG.6

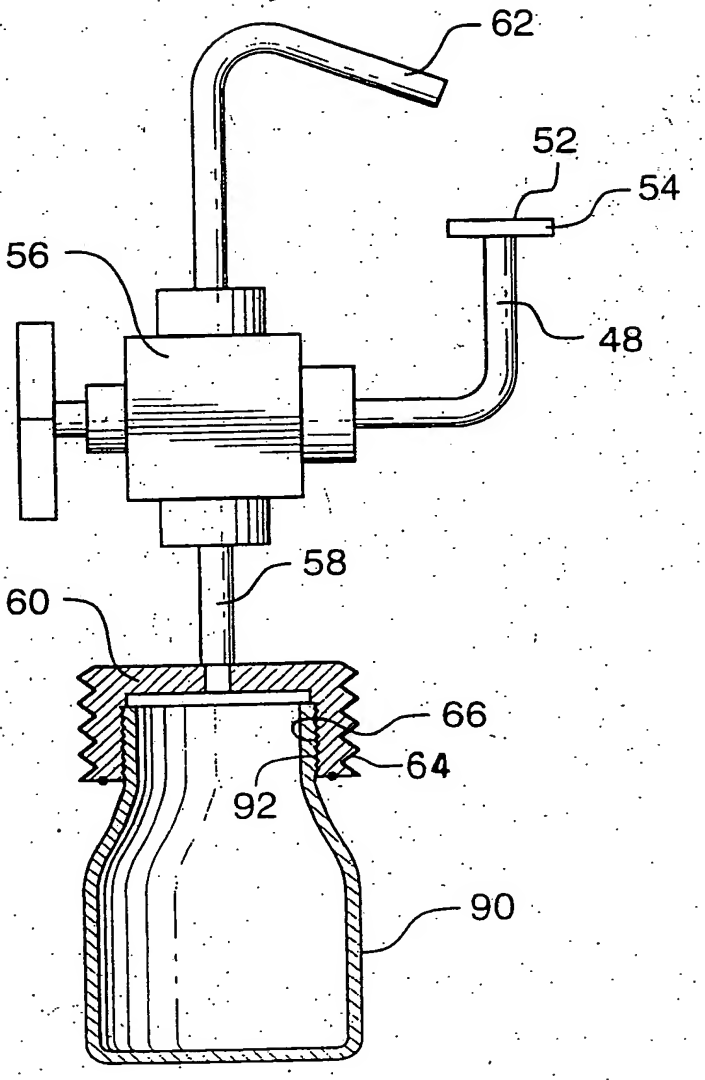
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FIG.7

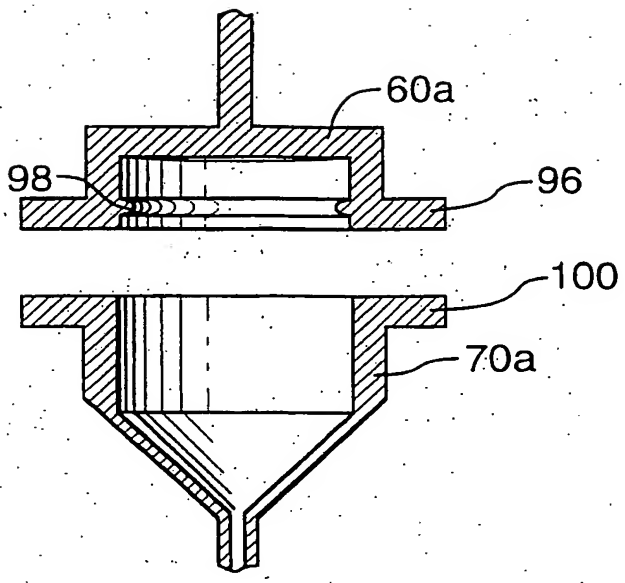

FIG.8

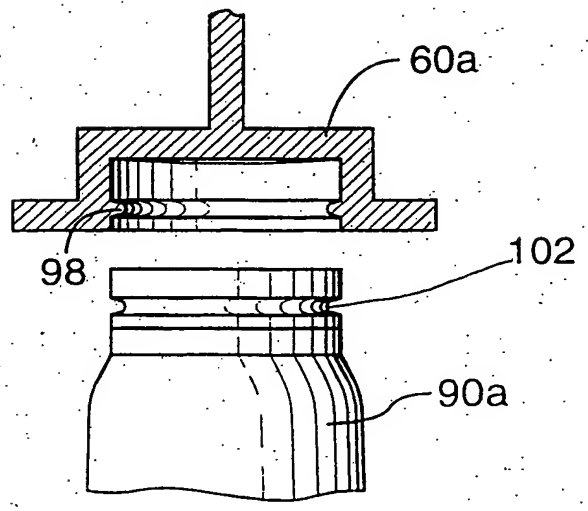

FIG.9

INTERNATIONAL SEARCH REPORT

I Application No
PCT/CA 99/00110

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12M1/26 C12M1/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2 566 306 A (S. C. BEESCH) 4 September 1951 (1951-09-04) column 2, line 34 - line 54; figures 1,2	1,4,5, 10,16, 32,33
A	US 3 075 888 A (G. B. ACHORN ET AL.) 29 January 1963 (1963-01-29)	
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Y	EP 0 357 998 A (KABLAU HOCHDRUCK ARMATUR MENTE) 14 March 1990 (1990-03-14) claims; figures	1,4,5, 10,16, 32,33
A	WO 85 03773 A (MEYER PIO) 29 August 1985 (1985-08-29)	

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 June 1999	28/06/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Coucke, A

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INTERNATIONAL SEARCH REPORT

[redacted] Application No
PCT/CA 99/00110

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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